

09/982.351

**REMARKS**

Applicant notes with appreciation the indication of allowable subject matter in Claims 38-43 and 54-58.

**Rejections under 35 USC §102**

Claims 22 and 53 remain rejected under 35 USC §102(b) as anticipated by the Jun Bulletin of the Korean Chemical Society 17(8), 676-678 (1996). Applicant respectfully submits that the current amendment to Claim 22 obviates this basis of rejection. As amended, the formula shown in Claim 22 does not allow the possibility of hydrogen for R<sub>1</sub>. The cited reference does not show compounds having a nitrogen bridge with further substituents (and not a hydrogen) at this position in the pyrimidine ring, and therefore does not anticipate the currently claimed compounds. Applicant respectfully requests withdrawal of this basis of rejection.

**Rejections under 35 USC §112**

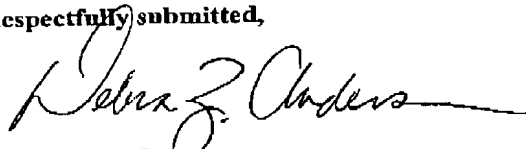
Claims 22, 36, 37 and 53 are again rejected under 35 USC §112, second paragraph, as indefinite for use of the term "*p*-aroyl-glutamate". Applicant respectfully submits that the term "*p*-aroyl-glutamate" is not unclear and is understood by one skilled in the art. This term indicates that the carbonyl-glutamate moiety on the aromatic ring is in the para position to the ring's site of attachment to the bridge compound, X<sub>2</sub>. In addition, one skilled in the art understands that an amide bond is formed with the glutamate; that is, the site of attachment of the aroyl group is through the nitrogen of the glutamate molecule. An exemplary compound of this formula is methotrexate, by its chemical name known as N-((2,4-Diamino-6-pteridiny)methyl)-methylamino)-benzoyl)-L-glutamic acid. Methotrexate is well known as the classic DHFR inhibitor, against which newer compounds are compared. The structure of methotrexate is shown in the Appendix attached following this response. As can be seen in the structure and the formula above, the benzoyl-L-glutamate moiety is in the para position to the site of attachment of the aromatic ring on the bridging carbon. Applicant respectfully submits that the term "*p*-aroyl-glutamate" is not indefinite and requests withdrawal of this basis of rejection.

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**SUMMARY**

As all outstanding issues have been addressed, Applicant respectfully submits that all pending claims, Claims 22, 36-43 and 53-58 are now in condition for allowance; such action is respectfully requested at an early date.

Respectfully submitted,



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## APPENDIX

N-(p(((2,4-Diamino-6-pteridiny)methyl)-methylamino)-benzoyl)-L-glutamic acid  
also known as methotrexate;

